Oestrogen plus progestogen did not prevent cardiovascular disease in postmenopausal women


Does oestrogen plus progestogen reduce the risk of coronary heart disease (CHD) in postmenopausal women?

**CONCLUSION**

In postmenopausal women, oestrogen plus progestogen was not cardioprotective and may slightly increase the risk of coronary heart disease, particularly during the first year of treatment.

A modified version of this abstract appears in ACP Journal Club.

**Commentary**

Cardiovascular disease is the leading cause of death among postmenopausal women.1 Evidence from previous observational studies suggested that hormone replacement therapy (HRT) offered some cardioprotective benefit, namely improved lipid profiles and slower progression of atherosclerosis.2 Large prospective randomised controlled trials (RCTs) now contradict these purported benefits of HRT. The Heart and Estrogen/progestin Replacement Study, the first large scale RCT, followed up 2763 postmenopausal women with known CHD over 4.1 years and concluded that HRT did not reduce non-fatal MI or CHD mortality.2,3 More recently, the Women’s Health Initiative (WHI) conducted the first large randomised primary prevention trial in apparently healthy postmenopausal women. At 1 year, women assigned to HRT had an 81% increased risk of non-fatal MI. However, over 5.3 years, this risk decreased to 28%.1 Discontinuation rates were 42% for the HRT group and 38% for the placebo group. An important trend towards a decrease in CHD for the study group and an increase for the placebo group may have been confounded by discontinuation rates. Thus, the reported risk for women who received HRT might have been underestimated.

Absolute rates of CHD in the WHI study were 39 and 33 cases per 10 000 person years for women treated with HRT and placebo, respectively. Thus, over 1 year, for every 10 000 women who take oestrogen plus progestogen, an additional 6 will have CHD events. An estimated 20 million women worldwide are taking HRT, and therefore as many as 120 000 women on HRT may be at risk of non-fatal MI or death caused by CHD.

The findings of the WHI reported by Manson et al confirm that HRT should not be recommended for primary prevention of CHD, although the effects of oestrogen as a single agent are unknown. However, for women with severe menopausal symptoms, HRT may be appropriate for short-term symptom relief on the condition that women are fully appraised of the risks of CHD and breast cancer.3 HRT should be prescribed on an individual basis, and re-evaluation with a physician is recommended, particularly during the first year when the associated risk of cardiac events appears to be highest.

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### Oestrogen plus progestogen vs placebo in postmenopausal women

<table>
<thead>
<tr>
<th>Outcomes at mean 5.3 years</th>
<th>Annualised percentage developing coronary heart disease (CHD)</th>
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<tbody>
<tr>
<td></td>
<td>Oestrogen plus progestogen</td>
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<tr>
<td>All CHD</td>
<td>0.39%</td>
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<tr>
<td>Non-fatal myocardial infarction (MI)</td>
<td>0.31%</td>
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<tr>
<td>Nonfatal MI (excluding silent MI)</td>
<td>0.31%</td>
</tr>
<tr>
<td>Death caused by CHD</td>
<td>0.08%</td>
</tr>
</tbody>
</table>

*CI defined in glossary. Hazard ratio adjusted for the presence or absence of previous coronary revascularization and sequential monitoring.
†Not significant.